CASE REPORTS

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March (Exertion) Hemoglobinuria

Report of Two Cases

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MARCH HEMOGLOBINURIA, a clinical condition characterized by dark brown pigmentation of the urine after strenuous marching or running, was first described by Fleisher in 1881. It occurs predominantly in men between the ages of 16 and 35 years[2, 3] and is entirely a separate entity from paroxysmal hemoglobinuria, in which syphilis is reported to be the causative factor.

In all reported cases except one, march hemoglobinuria was caused by exertion with the patient in an upright although not necessarily lordotic position. The exception was reported by Witts[7] who observed a patient in whom hemoglobinuria could be evoked by exercise on a bicycle ergometer and by running with the back acutely flexed.

The dark brown pigmentation usually is noted at the first but occasionally not until the second passage of urine following exercise, and the urine is of normal color between episodes. Many patients are completely comfortable during as well as between episodes. The syndrome is usually reported as spontaneously disappearing in from six months to two years.

No tenable theory of etiologic delineation has been evolved. Many investigators have expressed belief that the episodes of urinary pigmentation are preceded or accompanied by a rise in the content of hemoglobin in the plasma, which in turn results in hemoglobinuria. Palmer and Mitchell[5] offered a different concept: that hemoglobin which is normally and continuously discharged into the plasma by senile erythrocytes does not clear from the plasma at the time of the exercise, with the result that the plasma becomes surcharged with the substance. The majority opinion, however, is that behind the cause is either a hemolytic process (although circulating hemolysin has not been demonstrated) or a release of hemoglobin from erythrocytes owing to some change in the cell membrane that permits permeation.

In two cases observed by the authors the syndrome was precipitated not by marching or running but by violent jumping up and down. For this reason it is felt that the term *exertion hemoglobinuria* used by Lowbury and Blakely[4] more accurately describes the syndrome. The precipitating factor in all cases reported is exertion, differing only in kind —marching in some cases, walking or running in others and, as herein reported, jumping up and down.

CASE REPORTS

CASE 1. A 28-year-old man was first observed in January 1950 with complaint of occasional passage of brown urine. He related that for the preceding year immediately after leaving church services he passed brown urine. On succeeding days the urine would be clear and would remain so until the next attendance at church. The patient said that a part of the church ceremony consisted of shouting, handclapping and jumping up and down. There were no associated symptoms such as fever, chills or pain in the back. Upon physical examination the only abnormality noted was moderate tenderness of the prostate, which was not enlarged. The posture was normal.

Upon request, on the following Monday the patient submitted two specimens of urine, one collected soon after he left church and the other the next morning. The first specimen was reddish brown in color and the reaction to a test for albumin was 4 plus. Otherwise no abnormalities were noted on simple analysis. The second specimen was clear, normal in color and contained no albumin.

Further study of the urine to determine the pigmenting element and of the blood for possibly related information was contemplated, but the patient did not return until a year and a half later. With him was a friend who complained of severe pain in the back. In interview it was elicited that the friend attended the same church as the former patient and that he also passed brown urine after church services. Studies of both patients were then carried out concurrently (Table 1).

CASE 2. The patient, a 27-year-old man with complaint of excruciating pain in the back, said that for some five years he had had almost continuous pain, described as a drawing sensation, which was relieved somewhat by hyperextension of the back. About four years previously he had noted the passage of brown urine after he had played baseball rather strenuously. He had not noted the phenomenon again until he joined the previously mentioned church in 1949, but from then on the urine passed after attendance at church was brown.

Upon examination it was observed that the lower portion of the spine was acutely flexed anteriorly, owing to muscle spasm and pain. Several days later no pathologic condition of the back was observed upon examination. The range of motion was normal in all directions and there was no evidence of costovertebral tenderness in the lumbar region. The prostate was enlarged and moderately tender, and the left epididymis was enlarged but not tender. No abnormality was noted in an intravenous pyelogram.

Both patients were asked to submit specimens of urine

TABLE 1.—*Data on Studies of Urine and Blood After Exertion in Two Cases of Exertion Hemoglobinuria*

	Case 1	Case 2
Urine:		
Color	Dark brown	Dark brown
Specific gravity	1.019	1.022
Sugar	None	None
Albumin	3 plus	4 plus
Sediment	Few fine granular hyaline casts	Numerous granular hyaline casts
Pus cells	2 to 4 HPF	Occasional
Erythrocytes	None	Occasional
Methemoglobin	Present	Present
Oxyhemoglobin	Present	Present
Blood:		
Erythrocytes	5,100,000 per cu. mm.	4,740,000 per cu. mm.
Hemoglobin	14.5 grams per 100 cc.	13.1 grams per 100 cc.
Leukocytes	6,550 per cu. mm.	9,900 per cu. mm.
Distribution of leukocytes	Normal	Normal
Kolmer test result	Negative	Negative
Donath-Landsteiner reaction	Negative	Negative
Erythrocyte fragility	Normal	Normal
Sedimentation rate (Cutter)	9 mm. in 60 minutes	8 mm. in 60 minutes
Icteric index	5 units	17 units
Direct van den Bergh	.....	0.3 mg. per 100 cc.
Indirect van den Bergh	.....	0.9 mg. per 100 cc.

voided soon after the next church services and also to report immediately after services for withdrawal of specimens of blood. Laboratory data on the urine and the blood so obtained are given in Table 1.

The authors also attended the church to observe the patients at the services. During the singing of a hymn, continuously for eight minutes, both patients like others in the congregation became almost ineffably excited emotionally. With facial muscles taut in sardonic grin, they jumped and stamped rhythmically at ever increasing pace. The volume of voices was well-nigh deafening, the hand-clapping thunderous. The two patients, it was noted, threw their bodies into extremely lordotic position as they lifted arms and faces skyward in the classic attitude of supplication. Later another hymn, twice as long as the first and no less acrobatically fervid, was sung. It ended in sheer exhaustion of the participants.

TREATMENT

Gilligan and Blumgart[2] reported benefit in some cases in which the following means of treatment were used: (1) Maintenance of kyphosis during exertion, (2) alkalinization of the urine before exertion, and (3) administration of large doses of ascorbic acid.

Both patients here reported upon were given, at first, 500 mg. of ascorbic acid daily. After a week, the patient in Case 1 had no episodes of unusual urinary pigmentation. Therapy was discontinued at the end of a month, and passage of brown urine then recurred. Administration of ascorbic acid was resumed but at a dosage of 100 mg. daily, and there were no further episodes. The patient in Case 2 continued to have attacks even after a month of administration of 500 mg. of ascorbic acid daily. A starch-free "hyperacidity diet" and sodium bicarbonate tablets were then prescribed. When the episodes still did not abate, the patient was given 600,000 units of penicillin in oil intramuscularly every other day for two weeks. In the first week, although the patient attended church twice in that period, the color of the urine was normal. During the second week the episodes recurred and penicillin therapy thereafter seemed to have no effect.

Treatment must be empirical until more is learned about the basic cause of exertion hemoglobinuria. In this connection the authors' attention has been recently focused on the discoveries with regard to sickle cell anemia made by electrophoresis.[6] It is hoped that when Tiselius electrophoresis apparatus becomes available, similar studies can be made to determine if there is any departure from the normal in the hemoglobin of the two patients here reported upon.

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Combined Hormone Therapy of Pemphigus Vulgaris

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THE EMPLOYMENT of corticotropin (ACTH) or cortisone in the treatment of pemphigus vulgaris represents one of the major advances in the management of that disease. The use of these hormones has kept alive patients who heretofore undoubtedly would have died. The various investigators throughout the world who have reported successful treatment of patients moribund with pemphigus have been justifiably cautious not to claim any cures. The vast majority of patients with pemphigus vulgaris die within the first year of illness, yet some carry on with remissions and exacerbations for three years or longer, a variability that confounds evaluation of any therapy so far as cure is concerned. To indicate the improvement in prognosis with corticotropin and cortisone yet not imply that the hormones are curative, Sulzberger and Baer[6] coined the word *morbidistatic*.

In addition to other benefits, hormone therapy reduces the nursing load and greatly shortens the period of hospitalization. Many patients have been restored to productive lives by maintenance doses of corticotropin or cortisone. In some cases the disease has been controlled for many months, and there are reports of a few patients now in the second year of successful management.

In the following case, both corticotropin and cortisone were necessary for control of the disease.

REPORT OF A CASE

A 70-year-old white man with pemphigus vulgaris that had steadily increased in severity since onset some three months previously was observed by one of the authors in consultation late in March 1951. There were numerous intact and eroded bullae on the trunk, abdomen, buttocks, flexural surfaces of the elbows, on the sides of the neck, in the axillae and inside the mouth.

Naphuride chloride and large amounts of vitamin D had been given by mouth, without effect, and the bullous lesions on the trunk and extremities were being treated with potassium permanganate baths and a dusting powder. Cortisone

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